

Long-term Follow-up of Preoperative Infant Event-related Potentials in School-age Children with Craniosynostosis

Alexandra Junn, AB*
 Jacob Dinis, BS*
 Kitae E. Park, BS*
 Sacha Hauc, BS, MPH*
 Jenny F. Yang, MD*
 Carolyn Chuang, MD, BS*
 Gloria Han, PhD†
 James C. McPartland, PhD†
 John A. Persing, MD*
 Michael Alperovich, MD, MSc*

Background: Previous studies demonstrated impaired auditory processing in children with sagittal and metopic craniosynostosis before surgical correction. This study investigated whether worse presurgical neural response as assessed by event-related potentials (ERP) was predictive of poorer school-age neurocognition.

Methods: Preoperative infant ERP was recorded in 15 sagittal and 18 metopic patients. Mismatch negativity and P150 paradigms were derived from ERP recordings, as previously published. Of those, 13 sagittal and 13 metopic patients returned for neurocognitive evaluation 6 or more years later. ERP was correlated to neurocognitive outcomes using Spearman's correlations controlling for age. Two-tailed t-tests were used to evaluate the influence of age at the time of surgery (6 months) and morphologic severity on neurocognitive outcomes

Results: In the sagittal group, no significant correlations were found between preoperative mismatch negativity or P150 amplitudes and neurocognitive outcomes. Although no correlation was found between mismatch negativity and neurocognitive outcome in the metopic group, those with lower P150 amplitudes had higher scores in performance IQ ($r = -0.877$, $P < 0.001$) and full-scale IQ ($r = -0.893$, $P < 0.001$). Morphologic severity and neurocognitive outcomes showed no relationship in the sagittal or metopic groups. Patients who received surgery at less than 6 months had higher full-scale IQ (109.69 versus 95.92, $P = 0.025$), visuomotor integration (103.15 versus 90.46, $P = 0.041$), and visual perception scores (105.69 versus 96.08, $P = 0.033$).

Conclusions: Preoperative infant ERP does not correlate with school-age neurocognitive outcomes. Earlier age at the time of surgery was associated with improved neurocognitive outcomes. (*Plast Reconstr Surg Glob Open* 2021;9:e3844; doi: 10.1097/GOX.0000000000003844; Published online 4 October 2021.)

INTRODUCTION

Craniosynostosis is characterized by premature fusion of one or more cranial sutures, affecting one in 2000 to 2500 live births.¹⁻³ Fusion of the suture leads to impaired calvarial growth perpendicular to the suture, with a

compensatory increase in growth at the remaining patent sutures.⁴ This pathologic condition manifests in infancy, a critical time for calvarial expansion required for accommodating rapid development of the brain.

Auditory event-related potentials (ERP) from electroencephalogram (EEG) recordings are a noninvasive tool for assessing brain activity, and serve as a proxy for evaluating neural function in infancy. Detecting passive neural activity in response to speech sounds, auditory ERPs provide an objective measurement of cognitive function without requiring an overt behavioral response from the infant.⁵ Previous studies involving infant ERPs have demonstrated attenuated neural response to auditory

From the *Section of Plastic and Reconstructive Surgery, Department of Surgery, Yale University School of Medicine, New Haven, Conn.; and †Child Study Center, Yale University School of Medicine, New Haven, Conn.

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Drs. Junn and Dinis contributed equally to this work.

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stimuli in infants with sagittal^{6,7} and metopic⁸ craniosynostosis before surgical correction. Furthermore, more severe head shape deformity in metopic synostosis has been demonstrated to be correlated with reduced ERP responses.⁸

Limited evidence exists, however, illustrating how surgery affects neural response. One study comparing pre- and postoperative ERP values in infants with sagittal synostosis relative to controls showed the normalization of ERP values after surgery.⁶ The normalization of ERP following surgery suggests that surgical correction may restore previously aberrant neural function. At the same time, however, children with craniosynostosis exhibit persistent developmental deficits despite comprehensive surgical management.^{9,10} Thus, the extent to which preoperative neural deficits remain after surgery or improve after surgical correction continues to be the subject of debate.

This study used auditory ERPs to investigate whether the degree of presurgical attenuation of neural response correlated with poorer neurocognitive outcomes at school age. Given the correlation between the severity of morphologic deformity and ERPs in metopic craniosynostosis, we also sought to determine whether more severe presurgical morphologic deformity correlated with worse neurocognitive outcomes at school age after surgery.

METHODS

This study has been approved by the Yale Institutional Review Board (HIC#0804003650) and was initiated in

November 2010, in accordance with the Yale Human Investigations Committee with parental or legal guardian consent. Infants were recruited at the Yale Craniofacial Clinic if they had received a CT-scan confirmatory diagnosis of metopic or sagittal craniosynostosis.

ERP Analysis

Fifteen sagittal and 18 metopic synostosis patients underwent evaluations of auditory processing before surgery. Two distinct experimental paradigms were administered to derive two ERP waveforms: (1) a mismatch negativity (MMN) waveform and (2) a P150 waveform, with patients undergoing either one type or both types of analysis, as previously published (Fig. 1).^{6,8} During the experiment, each infant was seated in his or her parent’s lap or in an infant highchair. Participants were situated 90 cm from two loudspeakers, which delivered stimuli at 80 dB.

The experimental paradigm used in the MMN analysis consisted of a nonnative phoneme discrimination task. This paradigm involved equiprobable presentations of stimuli composed of either the Hindi retroflex or Hindi dental /da/. The MMN was computed as the largest negative amplitude in the difference wave obtained by subtracting the dental from the retroflex response between 80 and 300 milliseconds. The experimental paradigm used in the P150 analysis consisted of six English language phonemes: /ga/, /ba/, /da/, /gu/, /bu/, and /du/. The P150 wave consisted of the maximum amplitude between 100 and 300 milliseconds after the stimulus. All EEG was recorded

Preoperative ERP at infancy

Neurocognitive testing at school age

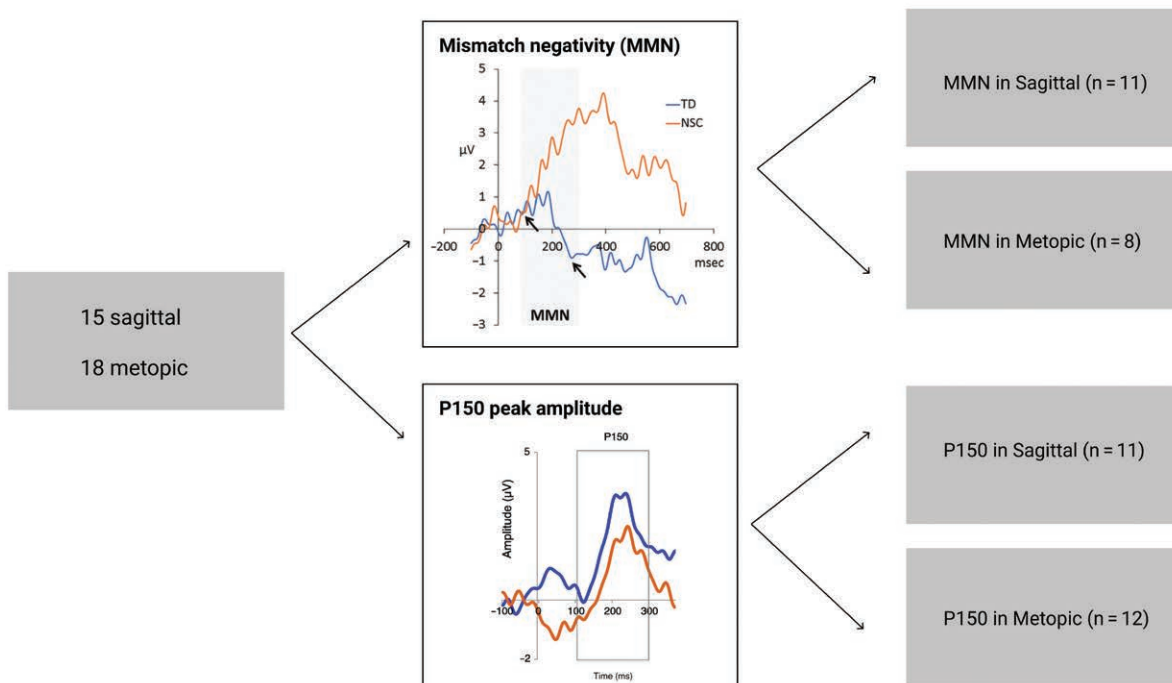


Fig. 1. ERP paradigms.

with an Electrical Geodesics, Inc. Net Amps 300 system using a 124-channel HydroCel Geodesic Sensor Net.

Morphologic Severity Quantification

Preoperative CT scans were obtained and analyzed using Mimics Materialise software (version 22.0, Leuven, Belgium). Severe deformity in the sagittal and metopic cohorts was defined as a cranial index less than 70.7 and an endocranial bifrontal angle less than 124 degrees respectively per prior definitions in the literature.^{11,12}

Neurocognitive Testing

Patients were contacted for neurocognitive testing at least 6 years following initial ERP evaluation. Of the patients who had been tested with ERP in infancy, two patients from the sagittal group were excluded because they were aged under 6 years. In the metopic cohort, two were excluded because they were aged under 6 years, one was excluded due to having a seizure disorder, one was excluded due to long-term hospitalization, and one declined participation.

Neurocognitive outcomes were assessed using a battery of neurocognitive tests, including measures of academic achievement in word recognition, math, reading comprehension, and spelling (Kaufman Test of Educational Achievement-3), verbal, performance, and full-scale IQ (Wechsler Abbreviated Scale of Intelligence II), and visual-motor coordination (Beery-Buktenica Developmental Test of Visual-Motor Integration VI). All tests were conducted by two trained administrators (AJ and JD) between September 2020 and January 2021.

Statistical Analysis

Correlations between preoperative ERPs and neurocognitive outcomes were assessed using partial Spearman’s correlations controlling for age. Additional correlations were done to evaluate demographic associations with neurocognitive outcomes. Partial Pearson correlations were assessed to examine the relationship between continuous demographic variables and neurocognitive outcomes while controlling for age at neurocognitive testing (eg, weight and neurocognitive test score). Associations between categorical demographic variables and neurocognitive test score (eg, race and neurocognitive test score) were assessed using partial ETA-squared measurements to estimate the amount of variance accounted for by the demographic variables while also adjusting for age at neurocognitive testing. Correction for multiple correlation analyses was performed using a Benjamini-Hochberg test. To assess differences in neurocognitive outcomes based on age and morphologic severity, we first dichotomized the age (<6 or >6 months) and morphologic severity variables based on clinically-informed thresholds, and then tested between-group differences using two-tailed *t*-tests. Strong correlation was set at *r* greater than or equal to 0.70 and *P* less than 0.05 as significant. SAS version 9.4 was used to analyze all relevant data.

RESULTS

In total, 13 sagittal and 13 metopic infants were followed up for neurocognitive evaluation at least 6 years

after ERP analysis. Of the sagittal patients, eight were White (61.5%), 11 were male (84.62%), and the mean age at surgery was 8.54 ± 9.08 months. The metopic cohort exhibited similar demographics with 10 White patients (76.92%), 10 male (76.92%), and a mean age of surgery of 9.29 ± 7.72 months. In terms of age at the time of neurocognitive testing, the sagittal patients were younger, with a mean age of 8.66 years compared with 9.29 years in the metopic group (Table 1).

In the sagittal group, no significant correlations were found between preoperative MMN or P150 amplitudes and neurocognitive outcomes (Tables 2–3). While no correlation was found between MMN and neurocognitive outcome in the metopic group (Table 4), those with lower P150 amplitudes had higher scores in performance IQ (*r* = -0.877, *P* < 0.001) and full-scale IQ (*r* = -0.893, *P* < 0.001; Table 5).

No significant differences or trends were identified between morphologic severity and neurocognitive outcome in the sagittal or metopic groups (Tables 6, 7). After correcting for multiple comparisons, there were no significant correlations between any of the demographic variables and neurocognitive outcomes. (See table 1, Supplemental Digital Content 1, which displays demographic associations in sagittal synostosis. <http://links.lww.com/PRSGO/B793>.) (See table 2, Supplemental Digital Content 2, which displays demographic associations in metopic synostosis. <http://links.lww.com/PRSGO/B794>.)

Table 1. Patient Demographics

	Sagittal (n = 13), n (%)	Metopic (n = 13), n (%)
Race		
White	8 (61.5%)	10 (76.9%)
Black	4 (30.8%)	1 (7.7%)
Hispanic	1 (7.7%)	2 (15.4%)
Gender		
Male	11 (84.6%)	10 (76.9%)
Female	2 (15.4%)	3 (23.1%)
Age at surgery, mo (mean ± SD)	8.54 ± 9.08	9.29 ± 7.72
Age at neurocognitive testing, y (mean ± SD)	8.66 ± 1.94	10.07 ± 1.56
Birth weight, lbs (mean ± SD)	7.74 ± 0.90	7.11 ± 2.29
Mother’s age at birth, y (mean ± SD)	29.08 ± 5.56	33.08 ± 7.09
Father’s age at birth, y (mean ± SD)	32.16 ± 5.51	36.33 ± 5.48
Breastfed? (yes)	9 (69.2%)	10 (76.9%)
Mother’s highest education level		
No high school	0 (0.0%)	1 (7.7%)
Completed high school	3 (23.1%)	1 (7.7%)
Some college/technical or associate’s degree	0 (0.0%)	8 (61.5%)
Completed college	5 (38.5%)	1 (7.7%)
Completed graduate school	5 (38.5%)	2 (15.4%)
Father’s highest education level		
No high school	0 (0.0%)	0 (0.0%)
Completed high school	4 (30.8%)	3 (23.1%)
Some college/technical or associate’s degree	0 (0.0%)	3 (23.1%)
Completed college	5 (38.5%)	4 (30.8%)
Completed graduate school	4 (30.8%)	2 (15.4%)
Income bracket		
<\$24,999	1 (7.7%)	1 (7.7%)
\$25,000–49,999	0 (0.0%)	1 (7.7%)
\$50,000–74,999	4 (30.8%)	4 (30.8%)
\$75,000–99,999	1 (7.7%)	0 (0.0%)
>\$100,000	7 (53.9%)	7 (53.9%)

Table 2. Spearman’s Correlations between Mismatch Negativity ERP Values in Preoperative Infants and Neurocognitive Scores at School-age in Sagittal Synostosis

	WR	Math	RC	Spelling	VIQ	PIQ	FSIQ	VMI	VP	MC
Frontal left										
<i>r</i>	-0.089	-0.101	0.298	-0.321	-0.187	-0.122	-0.062	-0.198	-0.454	-0.204
P	0.806	0.782	0.404	0.365	0.605	0.736	0.864	0.583	0.187	0.572
Frontal right										
<i>r</i>	-0.089	-0.193	-0.217	-0.229	-0.175	-0.449	-0.206	-0.205	-0.25	-0.292
P	0.807	0.594	0.547	0.524	0.629	0.194	0.567	0.571	0.486	0.413
Central left										
<i>r</i>	-0.296	-0.461	0.096	-0.46	-0.174	-0.339	-0.215	-0.344	-0.44	-0.568
P	0.407	0.18	0.792	0.181	0.631	0.337	0.55	0.33	0.204	0.087
Central right										
<i>r</i>	-0.429	-0.218	-0.303	-0.385	-0.331	-0.545	-0.417	-0.42	-0.187	-0.471
P	0.216	0.545	0.395	0.272	0.35	0.103	0.23	0.227	0.605	0.169

Table 3. Spearman’s Correlations between P150 ERP Values in Preoperative Infants and Neurocognitive Scores at School-age in Sagittal Synostosis

	WR	Math	RC	Spelling	VIQ	PIQ	FSIQ	VMI	VP	MC
P150 frontal L										
<i>r</i>	0.054	0.09	-0.423	0.423	-0.028	-0.166	-0.129	-0.162	0.047	-0.177
P	0.883	0.806	0.223	0.224	0.938	0.646	0.723	0.654	0.897	0.625
P150 frontal R										
<i>R</i>	0.108	0.291	0.457	0.196	0.297	0.56	0.388	0.073	0.312	0.18
P	0.767	0.415	0.184	0.588	0.405	0.092	0.268	0.841	0.38	0.618
P150 central L										
<i>R</i>	0.089	0.24	-0.456	0.431	-0.064	-0.183	-0.119	-0.205	0.027	-0.153
P	0.807	0.505	0.186	0.213	0.86	0.613	0.743	0.57	0.94	0.673
P150 central R										
<i>R</i>	0.535	0.342	0.494	0.578	0.348	0.657*	0.488	0.34	0.062	0.431
P	0.111	0.333	0.146	0.08	0.324	0.039	0.152	0.337	0.866	0.213

*Did not remain significant after correction for multiple comparisons.

Table 4. Spearman’s Correlations between Mismatch Negativity ERP Values in Preoperative Infants and Neurocognitive Scores at School-age in Metopic Synostosis

	WR	Math	RC	Spelling	VIQ	PIQ	FSIQ	VMI	VP	MC
Frontal left										
<i>r</i>	-0.233	0.12	-0.238	-0.179	-0.268	-0.146	-0.223	-0.352	-0.245	-0.638
P	0.616	0.798	0.607	0.702	0.561	0.755	0.63	0.439	0.596	0.123
Frontal right										
<i>r</i>	-0.22	-0.014	-0.62	-0.085	-0.38	-0.358	-0.387	-0.605	-0.432	-0.647
P	0.636	0.977	0.137	0.857	0.401	0.43	0.391	0.15	0.333	0.116
Central left										
<i>r</i>	-0.009	0.117	0.07	0	-0.217	-0.018	-0.117	-0.245	-0.095	-0.519
P	0.985	0.803	0.882	1	0.64	0.969	0.803	0.597	0.839	0.233
Central right										
<i>r</i>	0.154	0.248	-0.297	0.228	-0.205	-0.133	-0.191	-0.578	-0.371	-0.452
P	0.741	0.591	0.518	0.623	0.659	0.776	0.682	0.174	0.413	0.309

Table 5. Spearman’s Correlations between P150 ERP Values in Preoperative Infants and Neurocognitive Scores at School-age in Metopic Synostosis

	WR	Math	RC	Spelling	VIQ	PIQ	FSIQ	VMI	VP	MC
P150 L										
<i>r</i>	-0.002	-0.353	-0.407	-0.425	-0.148	-0.524	-0.464	-0.678	-0.522	-0.556
P	0.995	0.288	0.214	0.193	0.665	0.098	0.15	0.022	0.1	0.076
P150 R										
<i>r</i>	0.154	-0.522	-0.68	-0.271	-0.423	-0.877*	-0.893*	-0.715	-0.526	-0.631
P	0.651	0.1	0.021	0.419	0.195	<0.001	<0.001	0.013	0.096	0.037

*Remained significant after correction for multiple comparisons.

Table 6. Comparison of Neurocognitive Scores by Severity of Cranial Index in Sagittal Synostosis

	<70.7		>70.7		P
	Mean	SD	Mean	SD	
Word recognition	103.33	21.79	102.00	14.37	0.910
Math	101.17	18.57	103.80	15.77	0.808
Reading comprehension	98.17	15.56	103.80	19.72	0.608
Spelling	99.00	17.16	99.20	10.18	0.982
Verbal IQ	108.50	19.20	100.20	13.88	0.442
Performance IQ	105.17	9.87	111.20	18.77	0.510
Full-scale IQ	108.17	14.78	103.00	14.27	0.572
Visuomotor integration	105.00	10.47	89.20	19.58	0.120
Visual perception	104.50	6.29	99.00	7.21	0.209
Motor coordination	93.83	11.77	87.60	11.46	0.399

Table 7. Comparison of Neurocognitive Scores by Severity of Endocranial Bifrontal Angle in Metopic Synostosis

	<124 degrees		>124 degrees		P
	Mean	SD	Mean	SD	
Word recognition	104.83	12.703	104.67	8.595	0.979
Math	93.67	9.18	102.33	13.924	0.232
Reading comprehension	100.67	13.823	100.67	14.624	1.000
Spelling	95.83	9.131	102.5	13.576	0.342
Verbal IQ	97.17	6.585	103.67	10.482	0.227
Performance IQ	96.0	10.373	94.33	19.054	0.856
Full-scale IQ	95.83	6.113	98.0	16.26	0.770
Visuomotor integration	93.83	13.467	96.83	17.44	0.746
Visual perception	97.67	5.888	101.67	12.738	0.501
Motor coordination	88.17	16.327	85.83	17.128	0.814

When stratifying neurocognitive outcomes by age at the time of surgery, patients who received surgery at less than 6 months had higher scores in full-scale IQ (109.69 versus 95.92, $P = 0.025$), visuomotor integration (103.15

versus 90.46, $P = 0.041$), and visual perception (105.69 versus 96.08, $P = 0.033$; Fig. 2). An overall trend toward higher scores in the younger surgery group was observed for every testing category except for spelling, with verbal IQ also approaching significance (109.46 versus 98.92, $P = 0.087$; Table 8).

DISCUSSION

As a follow-up to our previous study using infant ERP in craniosynostosis, our results did not find a correlation between the degree of presurgical neural atypicality and eventual neurocognitive outcome. Besides two isolated neurocognitive outcome correlations with preoperative P150 amplitudes in infants with metopic synostosis, our results showed overall no correlation between preoperative ERP and neurocognitive outcome at school age. Thus, our results indicate that the degree of presurgical deficits in neural activity does not correspond to postoperative neurocognitive deficits at school age.

Our study conclusions are consistent with the findings of Chuang et al, which showed the normalization of ERP values following surgery.⁶ While the sagittal craniosynostosis infants in that study demonstrated significantly decreased MMN amplitude preoperatively compared with controls, there were no differences between the groups after surgery. Furthermore, there was also no relationship between pre- and postoperative ERP values in that cohort of patients. Our study supports the findings of Chuang et al, as ultimate neurocognitive performance was not a direct function of preoperative brain activity.

Studies using other modalities beyond ERP have also demonstrated that preoperative dysmorphology tends to normalize following surgery.^{13,14} In particular, results from

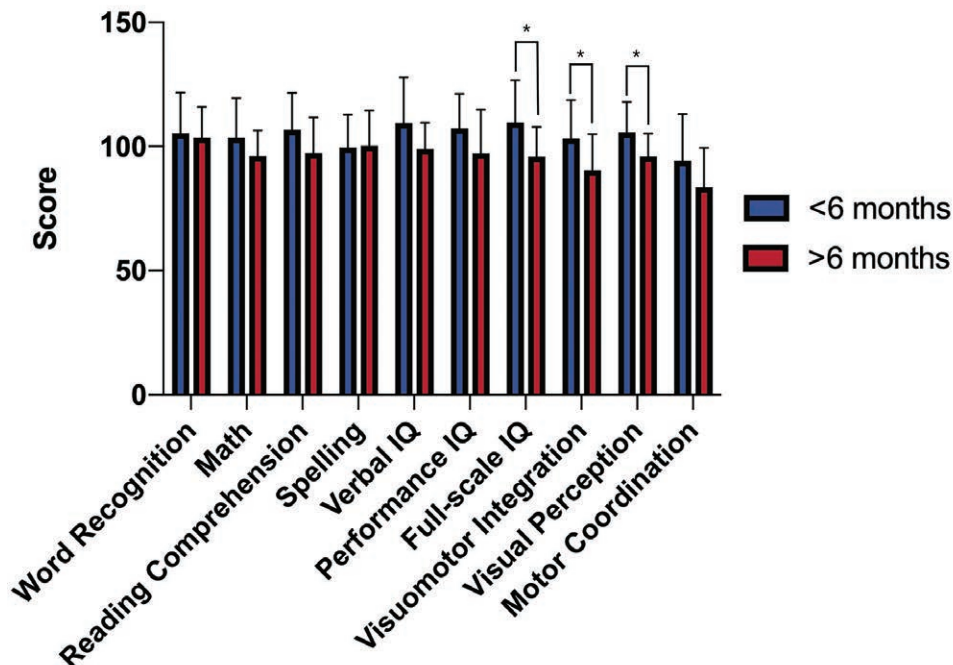


Fig. 2. Neurocognitive outcomes between patients receiving surgery before and after the age of 6 months. Asterisk values denote significance of $P < 0.05$.

Table 8. Comparison of Neurocognitive Scores by Age at the Time of Surgery in the Overall Cohort of Metopic (n = 13) and Sagittal (n = 13) Patients

	<6 Months		>6 Months		P
	Mean	SD	Mean	SD	
Word recognition	105.31	16.398	103.62	12.326	0.769
Math	103.62	15.814	96.15	10.335	0.167
Reading comprehension	106.69	14.924	97.31	14.361	0.115
Spelling	99.62	13.207	100.31	14.18	0.899
Verbal IQ	109.46	18.397	98.92	10.696	0.087
Performance IQ	107.31	13.913	97.23	17.527	0.118
Full-scale IQ	109.69	17.017	95.92	11.913	0.025
Visuomotor integration	103.15	15.486	90.46	14.512	0.041
Visual perception	105.69	12.264	96.08	9.133	0.033
Motor coordination	94.31	18.812	83.62	15.867	0.130

Values in boldface denote significance of $P < 0.05$.

deformation-based morphometry Jacobian mapping, which uses automated methods of objectively quantifying volumetric changes, showed no differences in surgically-treated adolescents with sagittal NSC compared with controls.¹⁵ Another study examining distances between 32 identifiable cortical and subcortical brain structures found that after surgery, the relative positions of structures in the brain still deviated from normal, although the overall brain shape reorganized to a morphology somewhere closer to normal, and where it was preoperatively.¹⁶ These findings are encouraging, as timely intervention may have permitted significant recovery even in those with more severe presurgical neural attenuation. In fact, synaptogenesis of the prefrontal cortex does not peak until 8 months, and continues through the first three years of life.¹⁷⁻²⁰ Our study results support the hypothesis that severity initial deformity may not have a corresponding level of deleterious long-term effect on neurocognition particularly if suture release occurs before the functional organization of higher-order processing centers.

The extent to which severity of presurgical morphologic deformity correlates to neurocognitive function remains an area of debate. Various indices of the severity of anatomic deformity have been suggested as risk

stratification tools, though a consensus on their utility has not yet been reached.^{11,12,21-24} In sagittal synostosis, no study to date has shown a relationship between degree of preoperative scaphocephaly and neurocognitive function. In a study of 75 children with sagittal synostosis, Ruiz-Correa and colleagues found no relationship between presurgical neurodevelopment or Preschool Language Scale and sagittal severity as measured by three different ratios of length to width.²⁵ In metopic synostosis, prior studies have had conflicting conclusions. Studies by Bottero et al,¹⁰ Yang et al,⁸ and Gabrick et al²⁶ have demonstrated an association between increased severity and worse neurodevelopment, whereas Warschusky et al,²⁷ Starr et al,²¹ and Mendonca et al²³ have shown no association between severity of trigonocephaly and cognitive development (Table 9).

In terms of understanding the competing effects on neurocognitive outcome in craniosynostosis, our results suggest that age at time of surgery may play a greater role than severity of initial deformity in eventual neurocognitive outcome. In the current study, infants receiving surgery at the age of less than 6 months performed better in every category except spelling, with significant differences found in full-scale IQ, visuomotor integration, and visual perception, whereas there were no differences when the groups were stratified by morphologic severity. Our results corroborate the work of prior studies demonstrating that earlier age at the time of surgery corresponds to improved eventual neurocognitive functioning later in life.^{10,28-30} Earlier screening may enable earlier detection of pathologic suture fusion. When possible, surgical teams considering timing of intervention for sagittal and metopic craniosynostosis should aim to complete the surgery before 6 months, which may minimize the potential neurodevelopmental impairment associated with delayed intervention.

The neuropsychology literature includes many previous studies validating the usefulness of ERP in infancy as a predictive tool for future neurocognition.³¹ This predictive value of ERP has been demonstrated in children with

Table 9. Review of Previous Studies Investigating Morphologic Severity and Neurocognitive Outcome

Study	n	Severity and Neurocognitive Assessment	Outcomes
Sagittal			
Kapp-Simon et al, 1993 ³⁷	65 infants between 18 and 36 mo	Cephalic Index; Bayley Scale, Preschool Language Scale	No association between CI and neurodevelopment
Ruiz-Correa et al ²⁵	75 children presurgery	Three ratios of cranial width to length; Bayley Scale, Preschool Language Scale	No relationship between skull shape and neurodevelopment in infancy
Metopic			
Bottero et al ¹⁰	76 children at >3 mo	Interparietal and intercoronal distance; psychologist and parent surveys to categorize level of mental development	Worse mental development with more severe frontal stenosis, with earlier operation being better
Warschusky et al ²⁷	22 infants between 3.6 and 25.3 mo	Plastic and neurosurgeon rating; Bayley Scale	No association between severity and cognitive development
Mendonca et al ²³	20 infants, assessed at 3 and 5 y	5 various preoperative measurements; speech and language assessments	No trend between severity and speech/language delay
Starr et al ²¹	65 infants between 18 and 36 mo	Trigonocephaly Severity Index; Bayley Scale, Preschool Language Scale	No association between TSI and neurodevelopment
Yang et al ⁴	16 infants, mean age 7.1 mo for severe, 7.0 mo for moderate	Endocranial bifrontal angle, ERP	Severity was associated with worse ERP
Gabrick et al ²⁶	20 patients, mean age 8.4 y for moderate, 10.8 mo for severe	Endocranial bifrontal angle, neurocognitive battery	More severe performed worse in word recognition and reading

normal neural function³² as well as in children with disorders such as dyslexia,³³ children born prematurely,^{34,35} and as a predictor for a positive outcome in comatose individuals.³⁶ Another interpretation of the outcomes in this study, however, could be that auditory ERPs are not a reliable predictor for future neurocognition in the craniosynostosis population. Nonsignificant correlations between preoperative ERPs and neurocognitive outcomes may be attributable to the limited resolution provided by ERPs. As ERPs measure the global distribution of an electric potential detected at various leads, they cannot resolve the activity of individual neurons or give information about neuron location or spatial orientation. Microstructural changes in patients with craniosynostosis may exist that were not detectable with ERP. As such, other modalities with higher resolution may be able to provide more granular details about the exact type of aberrancy in an individual with craniosynostosis.

Our study is also limited by the smaller sample size although there was limited attrition from the time of ERP to neurocognitive testing many years later. A larger sample would allow for a hierarchical regression analysis to formally test the incremental contribution of age at surgery and morphologic severity on neurocognitive outcomes. It is also possible that our study was not powered enough to detect a correlation despite its existence. Future studies investigating the relationship between postoperative ERP values and neurocognitive test scores with a greater number of patients could further clarify the findings presented here.

This study supports that aberrancies in neural function in craniosynostosis may be alleviated following surgery, with no strong correlation between preoperative ERP and neurocognitive outcomes at school age. Timely intervention may capture significant unrestricted growth to allow for adequate development of neural functioning.

CONCLUSIONS

The results of this study demonstrate that there is little correlation between preoperative ERP and school-age neurocognitive outcomes. Timely surgical intervention may permit normalization of brain function, and may play a greater role in ultimate neurocognitive outcome relative to initial deformity. Our study underscores the importance of early surgical intervention in correcting processing deficits.

Michael Alperovich, MD, MSc

Division of Plastic Surgery, Department of Surgery
Yale School of Medicine
330 Cedar Street, Boardman Building, 3rd Floor
New Haven, CT 06510
E-mail: michael.alperovich@yale.edu

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